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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/884,629	06/19/2001	Peter H. St. George-Hyslop	1034/1J800US1	3866

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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 03/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/884,629	ST. GEORGE-HYSLOP ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *8-23 and 29-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,24,25,27 and 28* is/are rejected.

7)☒ Claim(s) *26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application filed June 19, 2001, claims benefit to provisional application 60/212,534, filed June 20, 2000.

Applicants' request for a pre-appeal conference has been received. As noted in the response mailed December 12, 2006, prosecution has been re-opened.

Since this application is eligible for the transitional procedure of 37 CFR 1.129(a), and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action is hereby withdrawn pursuant to 37 CFR 1.129(a).

Claims 1-35 are pending.

Election/Restriction

Applicant's election with traverse of Group I, claims 1-7, 24-28, filed February 21, 2003, in Paper No. 9 was acknowledged. No new arguments have been provided, therefore the restriction is maintained for the reasons of record. The requirement is still deemed proper and is therefore FINAL.

This application contains claims drawn to an invention nonelected with traverse in Paper No. 9. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claims 1-35 are pending. Claims 8-23, 29-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9. Claims 1-7, 24-28 are currently under examination as they are drawn to a transgenic non-human mammal whose genome comprises a polynucleotide that encodes an amyloid precursor protein 695 transgene wherein the protein produced has the specific mutations in residues 670, 671 and 717 of APP_{695}.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 24-25, 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for transgenic mice which contain and expresses an APP_{695} transgene in their brains comprising an amino acid substitution at amino acids 670, 671, 717 operatively linked to a neuronal promoter, where the expression of the transgene produces abnormal Aβ deposition in the central nervous system of said mouse's brain, does not reasonably provide enablement for transgenic non-human mammals and the use of any type of promoter. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

At the time of the instant invention, the art taught that rats expression a truncated form of APP encoding the carboxyl terminal about 100 amino acids did not form any neuropathologies associated with Alzheimer's Disease or APP expression, although the rats did express the protein (Felsenstein, page 406, parag. 1). Also, at the time of filing a general unpredictability in producing transgenic mice that express an APP transgene sufficient to be a model for Alzheimer's Disease were thought to be that expression transgene to achieve the formation of Alzheimer's related symptoms may be difficult to achieve, and any expression achieved may show an inappropriate tissue distribution (Lannfelt, page 210, col. 1, parag. 5; and col. 2, parag. 4, lines 8-16). Applicant has clearly shown the production of mice with a particular transgene. Lannfelt's teachings support the limitation to the particular transgenes and to mice as the only embodiments enabled by the specification. While Lannfelt specifically discusses the unpredictable nature of producing transgenic mice models of Alzheimer's Disease, the unpredictability would be applicable to other mammals, and in particular to the category of

"rodent." It is a logical extension that which is unpredictable in mice would also be unpredictable in other mammals. Given these teachings, it was unpredictable at the time of filing that any non-human mammal could express any transgene or by any other means express APP resulting in the mammal having impaired memory or learning; or to develop abnormal neuropathology. Further, the specification only discloses the expression of a transgene to be the causative action in the production of mice that develop impaired learning or memory; or develop neuropathologies. The specification does not enable any other method of expressing amyloid precursor protein sufficient for the claimed phenotype. In addition, at the time of filing, the art recognized that the expression of human APP695 did not result in the production of any symptoms or neurological abnormalities over wild type mice (Higgins, page 225, parag. 1, lines 7-11). As the specification does not disclose features of the claimed invention necessary to develop the claimed phenotypes, and the specification only demonstrates such phenotypes associated by expression from the prion protein promoter, it would require and undue amount of experimentation to produce the mice as claimed. Further, the at the time of filing taught that as the prion promoter had been successful in producing transgenic mice expressing the prion protein coding sequence, and suggests the prion promoter as a means to over come the problems in producing transgenic mice as models for Alzheimer's Disease (Lannfelt, page 210, col. 1, parag. 6). The listing of other promoters does not provide the guidance necessary given the teachings in the art for the breadth of any promoter, in particular ones that are not active in the central nervous system of the mouse.

Applicant has taught wild type sequences and mutant sequences that would give rise to phenotypes. However, this is insufficient to provide guidance or teachings as to all means or all transgenes, which would give rise to such a phenotype in all non-human mammals as now

claimed. Further, the only transgenic nonhuman mammal comprising an amount of amyloid precursor protein disclosed is a transgenic mouse comprising a transgene comprising a mutant transgene. Further, mouse zygotes, embryos or progeny that do not develop into mice with a progressive neurologic disease phenotype(s) related to the expression of the transgene, have no use in view of the disclosure.

Thus, at the time of the present invention, the skilled artisan would have to perform an undue amount of experimentation without a predictable degree of success to make and use the transgenic nonhuman mammals claimed.

Claim Rejections - 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1, 2, 4-7 and 24- 28 rejected under 35 U.S.C. 102(e) as being anticipated by Hsiao *et al.* (US Patent 6,509,515) is withdrawn.

Upon review of Hsiao *et al.* it is found that all three mutations were known in the prior art and contemplated for use in generating transgenes for use transgenic models. However, there is no specific teaching to provide the specifically claimed combination of mutations in a single transgenic animal in Hsiao *et al.*

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4, 6-7, 24, 25, 27, 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hsiao *et al.* (US Patent 6,509,515).

It is noted that the claims broadly encompass the use of any promoter and no specific phenotype is recited to occur in the resulting transgenic animal. Hsiao *et al.* teach that all three mutations were known in the prior art and contemplated for use in generating transgenes for use transgenic models. As noted above, there is no specific teaching or reduction to practice by Hsioa *et al.*, however this does not overcome the fact that Hsiao *et al.* provides all the necessary teachings to generate the claimed transgenic animal. Moreover, as noted in the specification, the specifc combination of the three mutations were reduced to practice in the prior art , albeit with a different form of APP (page 11).

With respect to previous arguments regarding an unexpected results, it is noted that claims consistent with the unexpected results have not been included in the basis of the instant

rejection. Without the reduction to practice and the unpredictability of the art of transgenics, the specific outcome/phenotype can not be predicted precisely, however in view of the art of Alzheimer's Disease as a whole, there would be a general expectation that greater amounts of alterations associated with the disease would result in a more dramatic phenotype. Moreover, the unexpected phenotype is only demonstrated when expression is affected by one promoter and only in the mouse. In this case, consistant with Applicants remarks concerning the art of transgenics, the unexpected results would not extend to the use of any promoter and expression in any non-human mammal encompassed by the instant claims. However, as discussed above this is not found persuasive because each of the cited reference teaches that this APP mutation was known and contemplated for use in generating transgenic animal models of Alzheimer's Disease.

Conclusion

No claim is allowed.

Claim 26 is objected to for being dependent on a rejected claim. Claims 3, 5, and 26 are free of the art of record because while the art provides various genetic backgrounds for the resulting transgenic mice produced, none specifically teach any specific reason to generate (C3H xC57BL6) x C57 cross (claim 3). Further, it is noted that without the reduction to practice and the unpredictability of the art of transgenics, the specific outcome/phenotype can not be predicted precisely, in particular the deposition of placques in the central nervous system (claim 5) Moreover, the unexpected phenotype is only demonstrated when expression is affected by one promoter (see claim 26) and only in the mouse .

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach